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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/301,766	04/29/1999	EIJIRO WATANABE	0020-4559P	6045

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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/301,766	WATANABE ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,16-23 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,16-23,28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Office Action is in response to the Amendment and Remarks filed 30 August 2002.

2. The Examiner clarifies the typographical error in the previous Office Action, mailed 6 February 2002, item 2, line 4, the copending application to which the filed terminal disclaimer is directed is 08/992,914 and not 08/922,914.

3. The objection to the specification is withdrawn in view of Applicant's amendment.

4. The rejection of claims 1-10, 16-23 and 28-30 under 35 U.S.C. § 101 as lacking a specific and substantial asserted utility is withdrawn in view of Applicant's arguments on pages 9-12 of the Remarks. The Examiner will accept Applicants asserted specific utility for the instant claims. The rejection under 35 U.S.C. § 112, first paragraph, for enablement is maintained and is outlined below.

5. The rejection of claims 1, 16-22, 28, 29 and 30 under 35 U.S.C. § 102(e) as being anticipated by Osumi *et al* (U.S. Patent 6,166,292) is withdrawn in view of Applicant's amendments to the claims.

6. The provisional rejection of claims 1-3, 16-23 and 28-30 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 44-49, 54, 55 and 58 of copending Application No. 09/415,918 is now moot, said copending application appears to be abandoned.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

8. Claim 30 is objected to because said claim has been rewritten in independent form and is no longer dependent upon claim 1, thus the phrase "The isolated" should be amended to read -- An isolated --.

Claim Rejections - 35 USC § 112

9. Claims 1, 16-23 and 28-30 remain rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 6 February 2002. Applicant's arguments filed 30 August 2002 have been fully considered but they are not persuasive.

Applicant argues that the present application describes a plurality of isolated nucleic acids that encode raffinose synthase and provides a description of a method for obtaining an isolated nucleic acid encoding raffinose synthase "derived" from a plant selected from the group consisting of soybean, *Chenopdiaceae* plants and *Cruciferae* plants by performing a PCR reaction with one or more of a number of upstream and downstream primers (page 13, 3rd paragraph of the Remarks). This argument is not found to be persuasive, the Examiner notes that there are approximately 1,300 plant species in the *Chenopdiaceae* and 3,200 plant species in the *Cruciferae* plant families. It is evident from the instant specification that Applicant does not adequately describe such a broad genus of isolated nucleic acids, especially in light of the degenerate

nucleic acid sequences that encode diverse polypeptides having raffinose synthase activity. Applicant has not described specific molecular features that describe the claimed genus of raffinose synthase-encoding genes, only a functional characteristic that would be common to all plant raffinose synthase-encoding genes.

Applicant argues that the disclosure constitutes actual variants within the claimed genus and actual methods that can be used to find the next species within the genus and that the demonstration of isolation of three additional species of cDNA establishes predictability of obtaining additional species. Applicant also argues that the disclosure provides description of an assay that can be used to determine if the protein encoded by any gene isolated by the method of the Example in fact is a functional raffinose synthase (page 15 of the Remarks). This argument does not appear to be relevant to the instant rejection as directed to written description but does appears to support the Examiner's previous argument related to *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

10. Claims 1-10, 16-23 and 28-30 remain rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention. This rejection has been modified from that in the previous Office action mailed 6 February 2002.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

In the instant case, Applicant has provided limited guidance for isolating genes encoding plant raffinose synthase enzymes. The instant specification provides no evidence that Applicant has actually isolated a raffinose synthase gene. Applicant's assertion that Applicant has isolated raffinose synthase genes, at present, remains speculative. The art teaches that ultimately, the function of any DNA sequence, whose identity is based solely on homology, can only be proven by experiments designed to evaluate that function (Duggleby 1997, Gene 190:245-249, see page 248, left column, last paragraph). The state of the art is such that one of skill in the art cannot reasonably predict that a DNA sequence encodes a raffinose synthase enzyme based on the encoded amino acid sequence, and Applicant has provided no guidance on how one of skill in the art would reasonably predict such an enzyme function based solely on homology. Hence, given the limited guidance by Applicant, the teaching of the art at the unpredictability of the art it would have required undue trial and error experimentation by

one of skill in the art at the time of Applicant's invention to identify and isolate a myriad of DNA molecules that encode raffinose synthase enzymes from the myriad of species in the *Chenopdiaceae* and the *Cruciferae* plant families as broadly claimed.

If Applicant were able to provide evidence that the disclosed isolated nucleic acid molecules do in fact encode a plant raffinose synthase enzyme, the Applicant would be limited in scope to isolated nucleic acid molecules that encode the exemplified amino acid sequences (SEQ ID NOs: 1, 3, 5 and 7), compositions comprising said nucleic acid molecules and method of use. It cannot be predicted by one of skill in the art that nucleic acids that hybridize under certain stringency conditions will encode a protein with the same activity as that taught by Applicant. Bowie *et al* (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie *et al* teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column).

The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar *et al* (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract). Small changes in amino acid sequence can completely modify enzymatic function; Broun *et al* (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Lazar *et al* and Broun *et al* demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

11. Claims 1, 16-23 and 28-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At claims 1 and 30, line 2, the phrase "derived from" is indefinite because it is unclear how one derives a polynucleotide from a plant other than by isolating said polynucleotide and hence the metes and bounds of the claimed invention are unclear.

At claims 1 and 30, line 22, the phrase "under conditions equivalent to" is indefinite because it is unclear what the metes and bounds of the claimed invention are. The phrase appears to be suggestive.

At claims 1 and 30, lines 22-23, the "conditions" recited appear to claim stringency conditions for hybridization of nucleic acid molecules, yet said "conditions" do not appear to recite complete hybridization stringency conditions, such as binding

conditions and wash conditions and times, hence it is unclear what the metes and bounds of the claimed invention are.

Claims 16-23, 28 and 29 are also indefinite because they are dependent upon claim 1, and do not remedy the indefiniteness of claim 1.

Claim Rejections - 35 USC § 103

12. Claims 1, 16-22, 28, 29 and 30 are rejected and claim 23 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Osumi *et al* (U.S. Patent 6,166,292, filed 28 April 1997). This rejection has been modified and is repeated for the reason of record as set forth in the last Office action mailed 6 February 2002. Applicant's arguments filed 30 August 2002 have been fully considered but they are not persuasive.

Osumi teaches a nucleic acid isolated from a dicot, cucumber, that encodes a raffinose synthase enzyme (see claim 1) and an isolated DNA which originates from said dicot having an ability to produce raffinose from sucrose and galactinol which is hybridizable under Applicant's claimed conditions with said nucleic acid (see claim 2(b)). The isolated nucleic acids of Applicant's claims 1 and 30 would be hybridizable said conditions to the coding region of Osumi's SEQ ID NO:4. Osumi teaches a chimeric gene, plasmid, transformed microorganism and transformed plant comprising said isolated nucleic acid (see columns 22-24). Osumi also teaches a method of isolating the native raffinose synthase enzyme from cucumber in Example 1 at columns 16-18. Osumi teaches that one of ordinary skill in the art would be motivated to isolate raffinose synthase genes from other plants such as soybean, beet and rapeseed (*B. napus*) because regulation of the production of raffinose in said plants is desirable (see

columns 1 and 2). Additionally, Osumi teaches a method of isolating other raffinose synthase genes from other plants (see column 11, lines 30-64). Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to use the teachings of Osumi to isolate raffinose synthase genes from soybean, *Chenopdiaceae* plants or *Cruciferae* plants, transform plants with said isolated genes and isolate the expressed raffinose synthase.

Applicant argues that the protein expressed from the genes of claim 1 and 30 as amended are distinct from that taught by Osumi (page 17, 3rd paragraph of the Remarks). The Examiner as addressed this issue in the instant rejection as modified. Given the breadth of the claimed isolated nucleic acids, the Examiner asserts that it would have been obvious to isolate other raffinose synthase genes from the plants of the instant claims.

Applicant argues that Osumi does not suggest to modify the transformant expressing the protein of claim 23, and that the protein of Osumi originates from cucumber and does not suggest soybean, *Chenopdiaceae* plants or *Cruciferae* plants and thus does not render obvious the instant claims (paragraph spanning pages 17-18 of the Remarks). The Examiner responds that Osumi does suggest isolation of other raffinose synthase genes including those from of soybean, *Chenopdiaceae* plants and *Cruciferae* plants as broadly claimed. In addition, Osumi suggest isolation of the expressed raffinose synthase from a transformed organism (see column 12, lines 57-61). Thus, claim 23 remains obvious and claims 1, 16-22, 28, 29 and 30 are obvious in view of Osumi.

Double Patenting

13. Claims 1, 16-23 and 28-30 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-7, 13-17 and 21 of copending Application No. 09/612,095. This rejection has been modified and is repeated for the reason of record as set forth in the last Office action mailed 6 February 2002. Applicant's statement filed 30 August 2002, pages 18-19 of the remarks is noted. Applicant's traversal does not obviate the instant rejection. The issue of Double Patenting may be addressed in the instant Application at the time of allowance, and is dependent upon the status of the copending applications at such time.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR § 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. No claims are allowed.

16. Claims 2-10 appear to be free of the prior art because there is no disclosure or suggestion of the specific nucleotide sequences or polypeptides encoded by same.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

David H. Kruse, Ph.D.
6 November 2002